UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,649	07/28/2003	Lena Edelman	02356.0083	4213

22852 7590 10/18/2006

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,649	EDELMAN ET AL.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,46,52,59,64-66 and 68-90* is/are pending in the application.

4a) Of the above claim(s) *35,59-60,64-66,68, 85-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46, 52, 69-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to communication filed 7/25/2006. The status of the claims is as follows: claims 1-34, 36-45 47-51, 53-58, 61-63 and 67 are cancelled, claims 35, 46, 52, 59-60, 64-66 and 68-90 are pending, and claims 46, 52 and 69-84 are under current examination. Applicants elected species SEQ ID NOs: 239 and 269.

Applicant's election without traverse of Group IV in the reply filed on 7/25/2006 is acknowledged. While reconsideration of the application was requested, Applicant provided no indication of traverse.

Objection to the Specification

The disclosure is objected to because of the following informalities: "function" is spelled incorrectly on page 33 under Example 4.

Appropriate correction is required.

Claim Rejections

35 U.S.C. 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 46, 52 and 69-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aqeilan et al (1999), Kim et al (1997), US Pat. # 6713280 (hereinafter "Huang et al") and Sela and Zisman (1997). The limitations of the claims are:

1. A chimeric, bifunctional molecule comprising a molecule that targets and enters into the cell and a molecule that induces apoptosis via regulation of the PTPC;

2. The chimera comprising peptides as set forth in SEQ ID NOs: 239 and 269 and a peptide linker of 3 to 18 amino acids;

3. A pharmaceutical composition comprising the chimeric, bifunctional molecule above; and

4. wherein the chimeria comprises D-amino acids.

Aqeilan et al teaches a chimeric protein comprising an apoptosis-inducing protein, namely the human Bax protein for targeted therapy (whole document). While this prior art reference discloses a chimeric molecule with Bax to induce apoptosis for clinical purposes, it does not teach specifically teach either SEQ ID NOs: 239 or 269. Huang et al discloses a method of using peptides conjugates for the intracellular

targeting of the Bcl-2; the peptides include the amino acid sequence set forth in SEQ ID NO: 239 (see Table 2, column 10). Further, these peptides are utilized for inhibiting the anti-apoptotic function of Bcl-2 (see column 9, lines 29-42).

Although neither of the references disclose the *tat* component set forth in SEQ ID NO: 269, Kim et al disclose the unique ability of HIV-1 *tat* to transport macromolecules into cells and the shortest *tat* region of amino acids necessary for functional translocation. This motif is RKKRRQRRR (see Introduction), a motif found in SEQ ID NO:269. Kim et al also discusses the use of *tat*-conjugated proteins for the treatment of tumors and as a clinical utility (see Discussion). This reference discloses using a peptide spacer of a cysteine and three-alanines for conjugation of the chimera (see Methods).

The above references do not disclose peptide comprising D-amino acids. Sela and Zisman, however, state that "the inclusion of D-amino acids may be an advantage in terms of both specificity and efficacy, the latter because of longer persistence in an undigested for because they resist enzymatic degradation" (see abstract).

It would have been obvious to one of ordinary skill in the art to modify the methods taught by the above references in order to make a bifunctional, chimeric molecule comprising D-amino acids that enters cells and induces apoptosis. One would have been motivated to do so, as suggested by Aqeilan et al (1999), because killing cells via the apoptotic pathway minimizes any tissue damage or systemic response (see Discussion). There would have been a reasonable expectation of success given the knowledge that elevations in Bax protein levels are induced in several clinically relevant

settings where cell death occurs, including tumor cells during responses to chemotherapy and radiation, neurons following cerebral ischemia and myocardiocytes following acute mycocardial infarction (see Introduction in Aqeilan et al). Further, the crucial functional motifs of the *tat* protein are well characterized in the prior art as taught by Kim et al. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

CONCLUSIONS

In conclusion, no claims are allowed because all facets of the invention of the instant application are well-known in the prior art. Further, the specification fails to distinctly describe any novel functions of the peptide set forth in SEQ ID NO: 269 (*tat*) in addition to the already well-described motif.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday, 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 570-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for unpublished application is available through Private PAIR only. For more information about PAIR system, see htt://pair-direct.uspto.gov. Should you have questions on

access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michelle Horning
Patent Examiner

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600